Outbreak of acute colitis on a horse farm associated with tetracycline-contaminated sweet feed

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Abstract — Exposure of a group of horses to tetracycline-contaminated feed resulted in acute colitis and subsequent death in one horse and milder diarrhea in 3 others. The most severely affected animal demonstrated clinical and pathological findings typical of colitis X. The other herdmates responded well to administration of zinc bacitracin.

Résumé — Poussée de cas de colite aiguë sur une ferme équine associés à un aliment contaminé par la tétracycline. Parmi un groupe de chevaux ayant reçu un aliment contaminé par de la tétracycline, un animal a présenté une colite aiguë et est mort alors que 3 autres ont présenté une diarrhée moins sévère. L'animal le plus sévèrement atteint a montré des signes cliniques ainsi que des lésions pathologiques typiques de colite X. Les autres animaux ont bien répondu à un traitement à base de bacitracine de zinc.

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A 23-year-old, 500-kg Thoroughbred gelding was admitted to the Large Animal Clinic of the Ontario Veterinary College (OVC) for assessment and treatment of profuse bloody diarrhea of several hours' duration. The horse had been normal the previous day; however, on the day of admission, he was depressed and there was evidence of diarrhea in the stall. The diet had consisted of hay, pasture, and 2 kg of sweet feed daily. The only recent dietary change had been the acquisition of a new bag of sweet feed 2 d previously. There were 6 other adult horses at the farm.

Upon examination by the referring veterinarian, the gelding was depressed, tachycardic, clinically dehydrated, and had bloody, foul-smelling diarrhea. Palpation per rectum revealed gas-distended large intestines. Flunixin meglumine (1.1 mg/kg body weight (BW); Banamine, Schering-Plough Animal Health, Pointe-Claire, Quebec) and a balanced electrolyte solution had been administered, IV, prior to referral to OVC.

On physical examination at OVC, the gelding was exhibiting signs of septic shock: tachycardia (80 beats/min), congested and mildly cyanotic mucous membranes, a prolonged capillary refill time (> 5 s), and clinical dehydration approximating 10% of BW. Neither gastrointestinal sounds nor tympany was present upon abdominal auscultation, and the horse passed a small amount of bloody, foul-smelling diarrhea, which was followed by marked tenesmus. Palpation per rectum was not repeated due to the animal's obvious discomfort and mucosal irritation. A blood sample was obtained and results of blood gas and electrolyte concentration analysis showed a moderate metabolic acidosis (pH 7.28; normal, 7.36 to 7.43) with hypochloremia (88 mmol/L; normal, 96 to 102 mmol/L) and hyperkalemia (5.5 mmol/L; normal, 2.9 to 4.5 mmol/L). The packed cell volume was increased (80 L/L; normal, 30 to 40 L/L) and the total serum protein was within the reference range (60 g/L; normal, 60 to 75 g/L), although, given the state of dehydration, this was likely falsely increased due to hemoconcentration. Abdominocentesis was performed to rule out the presence of necrotic bowel or intestinal rupture and a serosanguinous fluid was obtained. The nucleated cell count was normal; however, the percentage of neutrophils was increased at 70%, as was the protein, at 66 g/L (normal, < 25 g/L), supportive of protein transudation from the bowel. Neither bacteria nor feed material was visible. A complete blood cell count and biochemical profile were performed and, in addition to the aforementioned abnormalities, increased urea and creatinine and creatinine kinase concentrations were present, likely due to prerenal azotemia and poor perfusion to the muscles, respectively. The differential diagnoses included colitis X, salmonellosis, acute clostridial colitis, and Potomac horse fever, although the last was considered least likely, due to the acute onset and the time of year. The gelding was administered hypertonic saline (4 mL/kg

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BW) by rapid infusion, followed by lactated Ringer's solution (5 mL/kg BW/h, IV). The gelding's condition gradually worsened, however, and the animal was euthanized 3 h after arrival.

On gross postmortem examination, the mucosa of the large colon was diffusely red-black and granular, and the wall markedly edematous. The contents were watery and red-black throughout. The small intestine was also edematous and the mucosa appeared hemorrhagic. On light microscopic examination, there was extensive ulceration and erosion of the colonic mucosa. Morphologic changes within the lungs, adrenal glands, kidneys, and small intestines were consistent with toxemia. The gross and microscopic pathological changes, together with the clinical signs, were consistent with a diagnosis of colitis X. Bacterial cultures of the colonic contents revealed a moderate number of *Clostridium perfringens* (unknown type) and *Escherichia coli* and were negative for *Salmonella* spp.

The day after the gelding died, 3 other horses on the farm developed anorexia and foul-smelling, soft to diarrheic, and, in 2 horses, hemorrhagic, feces. They, too, were fed sweet feed. The remaining horses on the farm were not fed sweet feed and were unaffected. The clinically affected horses were treated with oral zinc bacitracin premix (Zinc-Bacitracin, Rhone-Poulenc Canada, Mississauga, Ontario; active ingredient 110 g/kg feed), 50 mg, q12h for 24 h, followed by q24h for 2 d; all the horses recovered. Fecal samples were not submitted for anaerobic culture but were negative for *Salmonella* spp.

Analysis of the sweet feed revealed antibiotic residues of the tetracycline family at a concentration of 10 ppm (10 mg/kg) (Antimicrobial Residue Unit, Laboratory Services, University of Guelph, Guelph, Ontario). This dose is used as a growth promoter in swine rations, which were also formulated by the feed mill from where the sweet feed originated.

Antibiotic-associated colitis can range in severity from mild diarrhea to fatal colitis, typical of colitis X, a sporadic, acute, and severe disease of horses generally diagnosed at postmortem examination (1). Typical clinical signs of colitis X include severe, watery to hemorrhagic diarrhea, dehydration, abdominal pain, and toxic shock (2–5). Postmortem changes, which consist of mucosal edema and hemorrhagic necrosis, are most severe in the cecum and large colon, which contain watery to bloody ingesta (3,4). Antibiotics, as well as "stress factors" such as transport, illness, and surgery, likely initiate the disease by upsetting the normal anaerobic colonic flora. Antibiotics demonstrated clinically and experimentally to produce colitis X include tetracyclines, lincomycin, and erythromycin ethylsuccinate (2–4,6–8); however, only one other report has been associated with antibiotic feed contamination (2). Concentrations of drugs producing disease have ranged from subtherapeutic doses of erythromycin ethylsuccinate to doses of oxytetracycline surpassing therapeutic ranges (7,8). Difficulty arises in comparing the concentration of tetracycline in this case with that in reports of colitis X, since in the latter, oxytetracyclines were given parenterally.

A causative organism for both colitis X and antibiotic-induced colitis has not been definitively identified; however, an overgrowth of potentially pathogenic organisms, such as *Clostridium* spp., *Salmonella* spp., and/or *E. coli* is suspected (5). Experimental reproduction of colitis X has implicated *C. perfringens* type A as a potential pathogen, since it produces an enterotoxin that, when injected IV, produced colic, severe shock, and pathological changes typical of colitis X (9). *Clostridium perfringens* has also been cultured in large numbers from the feces and intestinal contents of horses succumbing to acute colitis following antibiotic therapy with oxytetracycline and erythromycin (7,8). *Clostridium difficile* was associated with an outbreak of diarrhea amongst horses in a veterinary hospital where all affected animals had received antibiotics (10). Other clostridial species have been associated with equine enterocolitis (reviewed in 11); however, their role in the pathogenesis remains controversial, as no study has shown conclusively that oral administration of *Clostridium* spp. has produced disease (11). Overgrowth of *E. coli* and the resultant release of endotoxins may also contribute to the toxic shock syndrome and subsequent death (5). In the fatal case we have described in this report, both *C. perfringens* and *E. coli* were cultured from the intestinal contents, so toxins from both may have contributed to the horse's demise.

Antibiotic-associated colitis can result in milder diarrhea, as seen in the other horses affected in this herd. Factors governing the severity of the disease when clostridial agents are suspected include the host's age and immune response, virulence of the infecting strain, and the degree of disruption to the normal intestinal defenses and microflora (11). The 2 horses with hemorrhagic diarrhea received different amounts of contaminated feed (a handful/d and 0.5 kg/d), suggesting that the above factors may indeed affect susceptibility to disease. Although the fatal case received more feed than the others, a dose-dependent affect of antibiotic on disease severity should not necessarily be concluded (7).

Although the involvement of *Salmonella* spp. in these cases cannot be ruled out, the fact that a *Salmonella* species was not identified in the fatal case and the less affected horses recovered with bacitracin treatment alone made it a less likely cause. Also, the horses not exposed to the sweet feed but maintained in the same environment remained healthy, suggesting an infectious cause was less likely. Multiple fecal samples (5) should have been submitted to determine conclusively that these horses were negative for *Salmonella* spp. Regardless of the specific agent involved, we believe it can be concluded that the antibiotic contamination of the feed led to an intestinal dysbacteriosis, resulting in death in 1 horse and milder colitis in 3 others.

If clostridial colitis is suspected in a herd outbreak of colitis, at least 25 g of feces should be submitted for *Clostridium* spp. toxin identification; however, a swab is sufficient for bacterial culture and multiple samples should be submitted (11). Toxins remain active in fecal specimens for 24 h, if refrigerated; however, samples should be frozen if submission to the laboratory is delayed (11). Recovery of large numbers of a single species is likely to be important in terms of etiology; however, isolation of *Clostridium* spp. in low numbers

may be but a marker for floral upset (11), suggesting an antibiotic residue or toxin is present.

Oral zinc bacitracin premix (25 to 50 g, q12h for the first day, then q24h for 4 d) and metronidazole (15 mg/kg, q8h for 3 d) have been used in association with supportive therapy to treat clostridial colitis with some anecdotal success (1,11). Zinc bacitracin is active against gram-positive organisms and is minimally absorbed from the intestines. It has been used successfully in a small number of experimentally-induced colitides (1). It can be administered by nasogastric tube or oral syringe (when mixed with molasses). The higher dose of bacitracin has been associated with reversible anorexia and large colon impaction in normal ponies (unpublished observations). Metronidazole is active against most gram-negative and many gram-positive anaerobic bacteria. Colic and anorexia are potential complications of its administration.

This report illustrates the association of tetracycline-contaminated sweet feed with colitis in susceptible horses and depicts the varying severity of disease. *Clostridium* spp. were suspected as the etiological agents. Treatment with oral zinc bacitracin can be rewarding; however, further case control studies and comparisons with metronidazole administration in treating clostridial colitis are warranted.

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